Review

Med Ultrason 2015, Vol. 17, no. 3, 361-366
DOI: 10.11152/mu.2013.2066.173.aig

Musculoskeletal ultrasound in the evaluation of Polymyalgia Rheumatica

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Abstract

Polymyalgia rheumatica (PMR) is a relatively frequent disease affecting individuals older than 50 years and is characterized by inflammatory involvement of the shoulder and hip girdles and the neck. Clinical manifestations are represented by pain and morning stiffness in this regions. An extensive and comprehensive assessment of the inflammatory status is crucial in PMR patients, including imaging evaluation. This narrative review reports the current available data in the literature about the role of musculoskeletal ultrasound in PMR.

Keywords: polymyalgia rheumatica, ultrasound, bursitis, tenosynovitis

Introduction

Polymyalgia rheumatica (PMR) is an inflammatory rheumatic condition that typically affects individuals older than 50 years, with incidence increasing with age. An Italian epidemiologic study reported an annual incidence rate of PMR over the period 1980–1988 of 12.7/100,000 [1-2]. The etiology of PMR remains unknown, although currently the role of both genetic and environmental factors, such as infections, has been hypothesized. Familiar aggregation has been described and genetic polymorphisms in human leukocyte antigen (HLA) genes and other genes in the field of immune regulation have been associated with PMR [3-6]. However, to date, no etiologic theory has been confirmed.

PMR is more frequent in caucasian population and is considered the second most common inflammatory rheumatic condition in the United States. The prevalence of the disease shows a North-South gradient, with a higher incidence in Northern than in Southern countries, including Italy [2]. Focusing on the clinical manifestations, PMR is characterized by pain and morning stiffness, longer than 45 min, involving the neck and the shoulder and hip girdles. Stiffness and pain are usually bilateral, worsen in the morning and improve with activity. Fatigue, malaise, anorexia, weight loss and fever are also common and are considered "constitutional symptoms".

An association between PMR and giant-cell arteritis (GCA) has been described and PMR has been identified in 40-60% of patients affected by GCA; on the contrary, GCA has been registered in 16-21% of patients with PMR [7].

An extensive and comprehensive assessment of the inflammatory status is crucial in PMR patients, including imaging evaluation. Musculoskeletal ultrasonography (MSUS) has acquired an increasing role over the recent years in the assessment and monitoring of rheumatic diseases. In fact, thanks to the progressive technological advances and the application of standardized scanning techniques and definitions of US pathology, its diagnostic capability has progressively increased [8]. MSUS is a multiplanar and dynamic imaging modality with several advantages: it is safe, feasible, relatively inexpensive and highly accepted by patients. The use of conventional B-mode US provides a wide set of information about the status of different musculoskeletal tissues. In addition, the development of power Doppler (PD) and color Doppler (CD) techniques has enhanced the abilities of US to detect and evaluate inflammatory joint activity [9].

Received 30.06.2015 Accepted 08.07.2015
Med Ultrason
2015, Vol. 17, No 3, 361-366
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This narrative review focuses on the analysis of currently available data in the literature about the role of MSUS in the assessment of patients affected by PMR.

Ultrasonography and PMR

In order to perform a comprehensive sonographic assessment of girdles in PMR patients, US examination should be focused on the evaluation of both intra-articular and extra-articular abnormalities, according to a standardized scanning method and published reference values [10-11].

At shoulder level, the most relevant inflammatory findings that should be investigated by US are represented by gleno-humeral synovitis, subacromial/subdeltoid (SAD) bursitis, and long-head-biceps tenosynovitis. Similarly to the shoulder, MSUS has a key role also in the assessment of the hip joint where the presence of synovitis can be demonstrated as well as the inflammatory involvement of local synovial structures (trochanteric, iliopsoas, and ischiogluteal bursae).

Ultrasonographic findings in PMR patients

In the last years, a number of studies have been performed to test the value of MSUS in detecting inflammatory lesions in PMR. As shown in table I, most of them were cross-sectional studies, were performed in Southern European countries (above all Italy) and described the main inflammatory US lesions at disease onset or during relapse. Except for the study of Zaccaria et al, they were conducted in small groups of PMR patients [12-28]. In terms of clinical assessment, when patients were investigated for the presence of symptoms, shoulder pain was the most frequent complain. In some cases, clinimetric tests (such as Visual Analogue Scale for pain, patient and medical global assessment, Health Assessment Questionnaire, and Leeb's Disease Activity Score) were also applied [18-20].

In terms of US assessment, all studies were conducted by using B-mode US and in two cases PD was additionally applied [19-21] . The shoulder was studied almost in all reports while the hip was assessed in few cases. An extensive polyarticular US examination was performed in two studies which were focused on the comparison between PMR and Rheumatoid arthritis (RA) [21-22]. Concerning the scoring system used for grading the severity of inflammatory lesions, in the majority of studies exclusively a binary assessment was applied [12,13,19,22-24]; in a few of them a semiquantitative 0 to 3 score was used [18, 25,26], and finally, in two cases both scoring methods were applied [21-27].

The most frequent US abnormalities were detected at shoulder level and were represented by SAD bursitis and

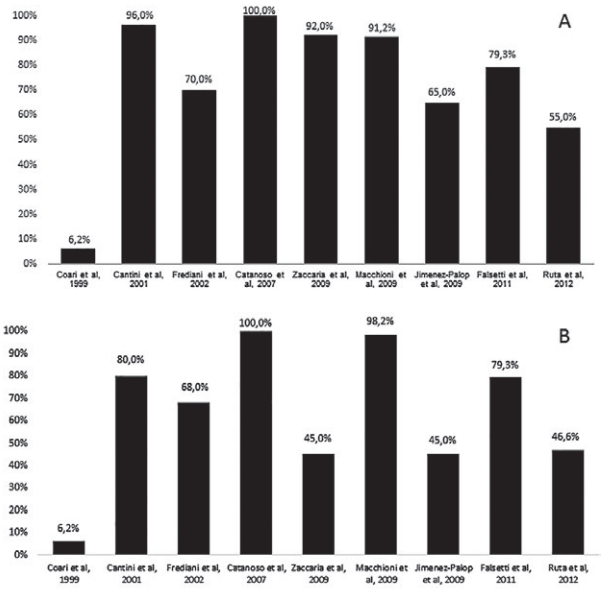

Fig 1. Distribution of the frequency of SAD bursitis (A) and LBT tenosynovitis (B) in the studies analyzed.

LTB tenosynovitis that have been reported in percentages ranging from 6.2%-100% (fig 1) [12-13]. However, the prevalence of SAD bursitis resulted higher compared to LBT tenosynovitis in the majority of the studies, suggesting this lesion as the inflammatory hallmark in PMR [13,18-20,22,25,26]. Moreover, as reported in Table I, a frequent US finding was the identification of bilateral involvement both at shoulder and hip level [19,21,25-27].

In terms of structures involved, the presence of SAD bursitis and LTB tenosynovitis was described as the most common finding in PMR patients, with a significant higher prevalence compared with RA subjects [13].

As shown in table I, few reports were conducted exclusively at hip level and, similarly to the shoulder assessments, extra-articular involvement was the most relevant finding with the evidence of trochanteric bursitis that was present in a significantly higher number of cases with PMR than in controls [27].

In terms of sensitivity two studies from the same research group comparing US to Magnetic Resonance Imaging (MRI) demonstrated that, at shoulder level, US-detected SAD bursitis was present in 96% of patients and that finding was confirmed in 100% of those individuals who underwent also MRI assessment [25]. At hip level, a sensitivity and specificity of 100% for US in detecting trochanteric bursitis, compared to MRI has been reported [27].

Concerning sensitivity to change, table II summarizes data obtained from the only three longitudinal studies reported in the literature, in which PMR patients underwent an US assessment at baseline and after starting treatment

Table I. Cross-sectional studies performed to test the value of MSUS in detecting inflammatory lesions in PMR

Study	Country	N. of patients	US scoring system	Power Doppler	Joints evaluated	US results
Lange et al, 1998	Germany	13	Dichotomic score *	No	Shoulders	GH synovitis: 61.5%
Coari et al, 1999	Italy	16	Dichotomic score *	No	Shoulders	GH effusion: 65.6% SAD bursitis: 6.2% LBT tenosynovitis 6.2%
Lange et al, 2000	Germany	22	Dichotomic score *	No	Shoulders	GH synovitis: 40.9 %
Cantini et al, 2001	Italy	57	Semiquantitative score (0-3)	No	Shoulders	GH synovitis: 77% (bilateral 45%) SAD bursitis: 96% (bilateral 96%) LBT tenosynovitis: 80% (bilateral 72%)
Frediani et al, 2002	Italy	50	Dichotomic score *	No	Shoulders, hips, ankles, wrists, elbows, knees, hands, feet	GH effusion: 66% SAD bursitis: 70% LBT tenosynovitis: 68%
Cantini et al, 2005	Italy	20	Dichotomic score * Bursitis: Semiquantitative-score (0-3)	No	Hips	CF synovitis: 45% trochanteric bursitis: 100% (bilateral 90%)
Catanoso et al, 2007	Italy	6	Semiquantitative-score (0-3)	No	Shoulders	GH synovitis: 33.3% SAD bursitis: 100% LBT tenosynovitis: 100%
Zaccaria et al, 2009	Italy	111	Semiquantitative score (0-3)	No	Shoulders	GH synovitis: 52% SAD bursitis: 92% (bilateral) LBT tenosynovitis: 45% (bilateral 34%)
Macchioni et al, 2009	Italy	57	Dichotomic score *	Yes°	Shoulders	GH synovitis: 15.8 % (bilateral) SAD bursitis: 61.4 % (bilateral) PD in SAD bursitis: 33% LBT tenosynovitis: 71.9 % (bilateral)
Jimenez-Palop et al, 2009	Spain	53	Dichotomic score *	No	Shoulders, hips	GH synovitis: 18% SAD bursitis:65% LBT tenosynovitis: 45% CF synovitis: 30%
Falsetti et al, 2011	Italy	29	All structures: dichotomic score * PDUS: semiquantitative score (0-4)	Yes	Hips, shoulders, elbows, wrists, MCPs, knees, MTPs	GH synovitis: 65.5% (bilateral 73.6%) SAD bursitis: 79.3% (bilateral 86.9%) LBT tenosynovitis: 79.3% (bilateral 78.2%) shoulder PDUS score > 0: 6.8% CF synovitis: 24.1% (bilateral 100%)
Ruta et al, 2012	Argentina	30	Dichotomic score *	No	Shoulders	GH synovitis 11.7% SAD bursitis: 55% LBT tenosynovitis: 46.6%

VAS = visual analog scale; MS = morning stiffness; HAQ = health assessment questionnaire; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; SAD = subacromial-deltoidea; LBT = long biceps tendon; GH = gleno-humeral; CF = coxo-femoral; PD = power Doppler; °in 24 patients; *presence/absence

Table II. Prospective studies performed to test the value of MSUS in detecting inflammatory lesions in PMR.

Study	Country	N	Joints evaluated	Treatment	Follow-up	Us results at follow-up
Catanoso et al. 2007	Italy	6	Shoulders	Etanercept 50 mg/week	24 weeks	50% decrease of inflammatory lesions
Macchioni et al. 2009	Italy	57	Shoulders	Prednisone (starting dose range 12.5-17.5 mg/day)	24 +/- 3 weeks	More than 50% decrease of inflammatory lesions
Jimenez-Palop et al. 2009	Spain	53	Shoulders hips	Prednisone (starting dose range 10-20 mg/day)	12 weeks	Normal in 50% of patients with lesions at baseline

GH = gleno-humeral SAD = subacromial-deltoidea; LBT = long biceps tendon; GH = gleno-humeral; CF = coxo-femoral; PD = power Doppler

for the disease [18-20]. Two studies, published in 2009, evaluated the modification of US features in more than 50 PMR patients, after 12 weeks [20] and 24 weeks [19] of treatement with glucocorticoids (prednisone). In both studies the therapy with steroids determined a significant decrease of the prevalence of inflammatory US features. Interestingly, the study published by Jimenez-Palop et al identified a significant improvement in US inflammatory lesions since week 4.

Previously, Catanoso et al in 2007 evaluated the response to Etanercept treatment in 6 PMR patients refractory to steroid therapy by using US assessment [18]. After 12 weeks of treatment, a 50% decrease in the prevalence of US features was registered in the enrolled patients, suggesting the possible positive effects of anti-Tumor Necrosis Factor drugs to treat PMR patients. This result underlined also the relevant role of US to demonstrate the efficacy of non-conventional treatment in PMR patients.

Concerning reproducibility, only one study assessed the intraobserver and interobserver reliability of US assessment in PMR patients, and demonstrated excellent results (k values 0.96 and 0.99, respectively) for both assessments [20]. However, the assessment was performed only on stored images and not on real-time US scanning thus limiting the reliability assessment to the interpretation of findings.

Three studies analyzed the correlations between US inflammatory findings and laboratory data [19,20,26]. No significant correlations between disease activity biomarkers and US findings were identified by Macchioni et al: in particular, at the evaluation performed at 24 weeks follow-up, 59.1% of patients in clinical remission or with low disease activity (Leeb's DAS < 7) showed persistent inflammatory lesions at the US evaluation [19]. Moreover, the studies conducted by Zaccaria et al and Jimenez et al in 2009 identified the absence of significant differences in the US pattern in patients with normal or high erythrocyte sedimentation rate (ESR). In addition, even in the presence of a parallel decrease in the findings, the authors did not find significant correlation between changes of clinical, laboratory and US parameters during the follow-up period [20,26].

In terms of predictive role of US in PMR patients, sonographic findings seem not able to predict the occurrence of disease relapses [19].

Currently available data suggest a relevant role of US as a diagnostic tool for PMR especially in the differential diagnosis with other rheumatic conditions with a possible polymyalgic onset and in the patients without typical laboratory abnormalities, such as increase of ESR. It is well known that PMR can mimic many other conditions, resulting in a difficult diagnosis and in the under-evaluation of serious diseases, such as tumors, infections, erosive arthritis. According with data from the literature, a shift in the diagnosis has been registered in 5-23% of patients complaining polymyalgic symptoms after a follow-up period of 12 months [14,15,28].

Falsetti et al in 2011 demonstrated an improvement of diagnostic sensitivity for PMR when US assessment was used, especially with the application of PD function. Sixty-one consecutive patients with clinical typical features of PMR underwent multi-district US evaluation at baseline and every three months. After a 12-months follow-up, a different diagnosis was made in half of patients (52%): specifically, they met classification criteria for elderly-onset rheumatoid arthritis, elderly onset spondyloarthritis, and calcium pyrophosphate deposition disease. The authors suggested a predictive model of US evaluation to classify PMR patients, including the presence of SAD bursitis, low frequency of wrist, metacarpophalangeal and metatarsophalangeal effusion/synovitis, low frequency of Achilles enthesitis, low frequency of knee menisci chondrocalcinosis, and tendinous calcaneal calcifications, and low hypervascularization at PDUS analysis in the wrist [19].

Morever, a percentage of PMR patients, ranging from 10 to 15% is reported as having a normal ESR. The study conducted by Zaccaria in 2009 analyzed this specific subset of patients, comparing them to typical PMR. No significant differences were described in the two groups of patients, concluding that US findings may help in the diagnosis of PMR more than laboratory features [26].

The primary role of US in the diagnosis of PMR patients determined the inclusion of this imaging tool in the new classification criteria, proposed by American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) in 2012 [16]. According to those criteria, US findings of bilateral shoulder abnormalities (SAD bursitis/LTB tenosynovitis/GH effusion) or abnormalities in one shoulder and hip (hip effusion, trochanteric bursitis) may significantly improve the specificity of the clinical criteria. Preliminary to the definition of the last classification criteria, some of the experts participating in the study assessed the inter-observer reliability in evaluating shoulders and hips abnormalities in PMR patients [16].

Conclusions

This narrative review confirms that MSUS is able to identify an extensive inflammatory involvement of extra-articular synovial structures in PMR patients. According

to data described in the literature, the presence of a typical MSUS pattern in PMR can be identified: the shoulder seems to be the most affected site, showing US lesions in a higher percentage compared with others rheumatic conditions and with healthy controls; SAD bursitis, especially when bilaterally, appeared to be the US lesion with the best diagnostic accuracy, followed by the presence of LTB tenosynovitis. Pelvic girdle is less frequently involved, with hip synovitis and trocanteric bursitis being the most relevant US lesions reported.

Generally, the depiction of bilateral abnormalities in both girdles achieves high specificity, but has low sensitivity. The presence of positive PD has been frequently reported, although this aspect has been investigated only in a few studies.

In order to improve the diagnostic accuracy, as reported in the recent classification criteria, US evaluation of shoulder and pelvic girdles is recommended in all patients with suspected PMR [27].

Conflict of interest: none

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